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STUDY EFFECTIVENESS OF TADALAFIL IN THE MANAGEMENT OF THE LOWER THIRD URETERAL STONES WITH SIZE 10 MM OR LESS

Kawa Mousa Daoud*[1] and Mohammed Kanaan[2]

[1]Master Degree in Urologic Surgery, Tishreen University Hospital, Lattakia, Syria.
[2]Supervisor, Professor in Urologic Surgery, Tishreen University Hospital, Lattakia, Syria.

***Corresponding Author: Kawa Mousa Daoud**

Master Degree in Urologic Surgery, Tishreen University Hospital, Lattakia, Syria.

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ABSTRACT

Study Aim: Study effectiveness of Tadalafil in the management of the lower third ureteral stones with size 10 mm or less. **Material and Methods:** The study sample consisted of (70) with a radiologically proven distal ureteral stone and were eligible for inclusion in this study and were systematically distributed into two groups: Group A: receive treatment with Tadalafil 5 mg once aday for 14 days. Group B: receive treatment with Placebo for 14 days. Tramadol or diclofenac potassium was also prescribed for pain relief. **Results:** The research sample comprised 70 patients, exhibiting a history of 5-10 mm lower ureteral stones confirmed radiologically during the period of 2023-2024. The patients' ages ranged from 19 to 69 years, with a mean age of 45.32±6.4 years. Stone sizes varied between 5 and 9.8 mm, Within the study sample, 75.7% were male (53 patients) and 24.3% were female (17 patients), Additionally, 72.9% (51 patients) had right-sided stones, In Group A, the average stone size was 6.9±1.9 mm, with sizes ranging from 5-9.8 mm; whereas, in Group B, the average stone size was 6.3±1.4 mm, with sizes between 5.3-9.1 mm. The average time for stone shedding in Group A was 5.8±1.8 days, with a range of 4-7 days. Conversely, Group B had an average shedding time of 9.66±2.6 days, with a range of 8-12 days. The stone shedding rate during the two-week follow-up period was 80% (28 patients) in Group A, while Group B recorded a shedding rate of 62.8% (22 patients).

KEYWORDS: Stones, urolithiasis, Tadalafil.

INTRODUCTION

Urinary calculi are a prevalent cause of hospitalization in the United States, with a lifetime incidence of 5-10%. The peak incidence occurs between the third and sixth decades of life, with a notable male predominance, as evidenced by a ratio ranging from 1.8:1 to 3.8:1.[1] The incidence rises in warmer regions due to factors such as dehydration and hypercalcemia linked to increased vitamin D synthesis. Vegetarian diets are associated with a fivefold lower incidence, whereas calcium replacement therapy in women correlates with an increased risk. Family history of urinary calculi significantly elevates the incidence rate by 2.5 times.[2] The recurrence rate is 7% annually and reaches 50% within a decade.[1]

Renal colic often serves as the first symptom of urinary stones, characterized by flank pain accompanied by nausea, vomiting, and occasionally fever in cases of infection. Patients may have a history of previously diagnosed stones. Severe flank pain typically occurs as a kidney stone passes into the ureter, presenting as sudden, colicky pain that may radiate to the groin. While pain location does not definitively indicate stone position, discomfort in the penis with an urgent desire to urinate may indicate a stone in the interstitial ureter.[3] Clinical diagnosis should be corroborated with appropriate procedures to facilitate timely intervention. Radiological investigations are essential for diagnosing urinary stones, with intravenous urography (IVP) historically considered the gold standard for identifying urinary stones and associated anatomical abnormalities. However, computed tomography (CT) scans now provide a rapid and effective alternative that does not require contrast material. Most practitioners regard simple radiography of the kidney, ureter, and bladder (KUB) combined with ultrasound imaging (US) as optimal for evaluating patients with flank pain.[4]

Pharmacological management is integral to treating urinary calculi, particularly in alleviating pain from ureteral obstruction. A variety of pharmacological interventions exist to assist in stone passage. Preventive measures are critical, especially for those at risk of developing calcific, cystine, or uric acid stones, particularly in the presence of infection.[5] One category of drugs employed in the management of ureteral stones comprises phosphodiesterase (PDE) inhibitors. PDE inhibits the breakdown of cyclic guanosine

monophosphate (cGMP) and cyclic adenosine monophosphate (cAMP), maintaining their active forms. Phosphodiesterase type 5 (PDE5) inhibitors, in particular, enhance cGMP levels within tissues and cells, activating nitric oxide (NO) within vascular endothelial cells to stimulate guanylate cyclase (GC), further driving the conversion of guanosine triphosphate (GTP) to guanosine monophosphate (GMP).[6-7]

Tadalafil, a selective PDE5 inhibitor, is primarily absorbed orally, achieving peak concentration two hours' post-dose, with an average half-life of 17 hours. It undergoes hepatic metabolism and is excreted predominantly in feces and to a lesser extent in urine. While primarily indicated for the treatment of erectile dysfunction, it has recently received approval for managing lower urinary tract symptoms associated with benign prostatic hyperplasia and lower ureteric stones.

Contraindications for tadalafil include hypersensitivity to the drug and its use in conjunction with nitroglycerin. Possible side effects may include flushing, hypotension, angina pectoris, myocardial infarction, palpitations, headache, weakness, dizziness, vertigo, nasopharyngitis, and nasal congestion. The most frequently reported adverse effects are nasal congestion, headache, and indigestion.[8-9-10]

METHODS AND MATERIALS

After obtaining the necessary official approvals, a comprehensive medical history was obtained from patients, who were subsequently divided into two groups based on admission criteria.

- Group One: Patients received tadalafil 5 mg once daily for 14 days.
- Group Two: Patients did not receive any pharmacological treatment.

Pain relief was provided through tramadol or diclofenac potassium. Laboratory tests, including urine and sediment examinations, kidney function assessments, and complete blood counts, were conducted. Radiological investigations included simple X-ray (KUB), ultrasound imaging of the urinary system (US), intravenous contrast imaging (IVP), and non-contrast axial computed tomography (CT).

Patients were monitored for stone expulsion into the bladder or external passage through symptom resolution and radiological validation (CT, KUB, US). Follow-up evaluations were performed to confirm stone expulsion and to accurately ascertain the expulsion timing. A simple X-ray (KUB) was conducted one week later for patients whose stone expulsion status could not be determined. The treatment was deemed successful if the stone was expelled within a 14-day treatment period or less. Conversely, the treatment was classified as a failure if expulsion did not occur.

Statistical Analyzes was done using IBM SPSS version 26, with significance when P value <0.05.

RESULTS

The research sample comprised 70 patients who visited the urology clinic and the emergency department of Tishreen University Hospital in Lattakia, exhibiting a history of 5-10 mm lower ureteral stones confirmed radiologically during the period of 2023-2024. These patients met the inclusion criteria for the study.

The patients' ages ranged from 19 to 69 years, with a mean age of 45.32±6.4 years. Stone sizes varied between 5 and 9.8 mm, averaging 6.97±1.5 mm. Within the study sample, 75.7% were male (53 patients) and 24.3% were female (17 patients), resulting in a sex ratio (M:F) of 3.1:1. Additionally, 72.9% (51 patients) had right-sided stones, while 27.1% (19 patients) had left-sided stones.

Statistical analyses indicated no significant differences between the two groups concerning gender, average age, or side of injury.

In Group A, the average stone size was 6.9±1.9 mm, with sizes ranging from 5-9.8 mm; whereas, in Group B, the average stone size was 6.3±1.4 mm, with sizes between 5.3-9.1 mm. No statistically significant differences were observed between the two groups regarding stone size, noting that Group A (tadalafil group) had a slightly larger average stone size.

The average time for stone shedding in Group A was 5.8±1.8 days, with a range of 4-7 days. Conversely, Group B had an average shedding time of 9.66±2.6 days, with a range of 8-12 days. Statistically significant differences in shedding time favored Group A, with an average of 6.1±1.8 days as opposed to 9.66±2.6 days in Group B.

The stone shedding rate during the two-week follow-up period was 80% (28 patients) in Group A, while Group B recorded a shedding rate of 62.8% (22 patients). Significant differences were noted between the two groups regarding treatment success rates, with Group A exhibiting higher success compared to Group B.

DISCUSSION

No statistically significant differences were identified between the two groups in relation to gender, age, stone size, or location of injury, with male patients and right-sided injuries predominating in both groups, and an average stone size of approximately 7 mm.

A statistically significant difference was observed in the percentage of elimination after 14 days, with rates reaching 80% in Group A compared to 62.8% in Group B. Furthermore, significant differences were noted in average elimination time, which was 5.8±1.8 days in Group A versus 9.66±2.6 days in Group B.

Among the seven patients who did not respond to

treatment, ureteroscopy was performed while continuing pain management as required. During the waiting period, four patients expelled their stones spontaneously, while three underwent successful ureteroscopy for stone removal.

Consequently, the study demonstrates considerable efficacy for tadalafil in the treatment of lower ureteral stones. A comparison with Hasan E Hasanain's[11] study indicated agreement in the number of successful cases in the tadalafil cohort (28 patients) and the average passage time (5.5 days). However, Hasanain's[11] higher success rate of 93% can be attributed to a smaller sample size (30 patients) compared to our study (70 patients).

In contrast to Abhishek Laddaha's[12] study, which recorded an 80% passage rate but utilized a higher tadalafil dosage (10 mg), our findings reflect differing patient group sizes. Hari Bahadar's[13] study indicated a slightly higher elimination rate of 84%, likely due to the higher tadalafil dose of 10 mg used, though his average elimination time was longer (8 days) due to larger stone sizes (7.13 mm).

Serdar Celik's[14] study, using a similar tadalafil dosage of 5 mg, aligned with our findings regarding the number of patients who successfully passed stones (27) and the average time (5.7 days), but his elimination rate (90%) was higher, possibly due to smaller stone sizes (4.7 mm) and a smaller patient cohort (30 patients).

CONCLUSIONS

Our study, corroborated by international research, affirms the efficacy of tadalafil in facilitating the passage of lower ureteral stones, particularly those sized 10 mm or less. We recommend the utilization of tadalafil for treating lower ureteral stones and propose further studies to evaluate the effects of varying tadalafil dosages, as well as its combination with other medications such as tamsulosin and prednisolone.

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REFERENCES

1. Marshall L. Stoller and Maxwell V. Meng. The Practical Guide to Medical and Surgical Management, 694., illustrated. Totowa, NJ, Humana Press, 2007.
2. Davison AM, Cameron JS, Grunfeld J-P,Kerr DN, Ritz E, Winearls CG, eds. Oxford textbook of clinical nephrology. 3rd edn. Oxford: Oxford University Press, 2005; 1201-1223.
3. Preminger GM, Tiselius HG, Assimos DG, Alken P, Buck AC, Gallucci M, Knoll T, Lingeman JE, Nakada SY, Pearle MS, Sarica K, Türk C, Wolf JS Jr; American Urological Association Education and Research, Inc; European Association of Urology. 2007 Guideline for the management of ureteral calculi. Eur Urol, 2007; 52(6): 1610-1631.
4. Preminger GM, Tiselius HG, Assimos DG, Alken P, Buck AC, Gallucci M, Knoll T, Lingeman JE, Nakada SY, Pearle MS, Sarica K, Türk C, Wolf JS Jr; EAU/AUA Nephrolithiasis Guideline Panel. 2007 guideline for the management of ureteral calculi. J Urol, 2007; 178(6): 2418-2434.
5. Hans Goran Tiselius. Medical treatment of patients with urolithiasis. department of urology, Karolinska university, Stockholm Sweden.
6. Francis S.H., Blount M.A., Corbin J.D. Mammalian cyclic nucleotide phosphodiesterases: Molecular mechanisms and physiological functions. Physiol. Rev., 2011; 91: 651–690.
7. Lin C.-S., Lin G., Xin Z.-C., Lue T.F. Expression, distribution and regulation of phosphodiesterase 5. Curr. Pharm. Des., 2006; 12: 3439–3457.
8. Lin C.-S., Lin G., Xin Z.-C., Lue T.F. Expression, distribution and regulation of phosphodiesterase 5. Curr. Pharm. Des., 2006; 12: 3439–3457. doi: 10.2174/138161206778343064..
9. Hossein Karami, Amin Hassanzadeh-Hadad, Morteza Fallah-Karkan, Comparing Monotherapy with Tadalafil or Tamsulosin and Their Combination Therapy in Men with Benign Prostatic Hyperplasia: A Randomized Clinical Trial, Miscellaneous, 2016.
10. Dig Vijay Singh, MS, MCh, Uttam Kumar Mete, MS, DNB, MCh, FRCSEd, Arup Kumar Mandal, MS, MCh, and Shrawan Kumar Singh, MS, MCh. A Comparative Randomized Prospective Study to Evaluate Efficacy and Safety of Combination of Tamsulosin and Tadalafil vs. Tamsulosin or Tadalafil Alone in Patients with Lower Urinary Tract Symptoms due to Benign Prostatic Hyperplasia, J Sex Med., 2014.
11. Arcangelo Sebastianelli, Pietro Spatafora, Jacopo Frizzi, Omar Saleh, Maurizio Sessa, Cosimo De Nunzio, Andrea Tubaro, Linda Vignozzi, Mario Maggi, Sergio Serni, Kevin T. McVary, Steven A. Kaplan, Stavros Gravas, Christopher Chapple and Mauro Gacci, Tadalafil 5 mg Alone or in Combination with Tamsulosin 0.4 mg for the Management of Men with Lower Urinary Tract Symptoms and Erectile Dysfunction: Results of a Prospective Observational Trial, Journal of Clinical Medicine, 2019.
12. The Role of Tadalafil in Lower Ureteric Stone Expulsion Hasanain F. Hasan,Waleed N. Jaffal, Harith A. Al-Hossona, 2011.
13. Dr Abhishek Laddha, Dr. Shashikant Mishra, Dr. Arvind Ganpule, Dr.Ravindra Sabnis, Dr. Mahesh Desai.Comparison of Tadalafil and Tamsulosin in Medical Expulsive Therapy for Ureteric Calculus: Prospective, randomized, placebo, 2019.
14. Tamsulosin versus tadalafil as a medical expulsive therapy for distal ureteral stones: A prospective randomized study. Hari Bahadur KC, corresponding author Anil Shrestha, Ganesh Bhakta Acharya, Robin Bahadur Basnet, Arvind Kumar Shah, and Parash Mani Shrestha, 2016.

15. Tadalafil versus alpha blockers (alfuzosin, doxazosin, tamsulosin and silodosin) as medical expulsive therapy for < 10 mm distal and proximal ureteral stones. Serdar Çelik 1, Firat Akdeniz, Muge Afsar Yildirim, Ozan Bozkurt, Merve Gursoy Bulut, Mehmet Levent Hacihasanoglu, Omer Demir, 2018.